Colon Cancer Screening Update and Management of the Malignant Polyp

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ABSTRACT

Colorectal carcinoma is common, but screening for this cancer has found less acceptance with the public than screening for breast, prostate, and cervical cancer. Available methods include fecal occult blood tests (FOBTs), flexible sigmoidoscopy (FOS), double-contrast barium enema, colonoscopy, computed tomographic colography, and fecal DNA. Evaluation of these options demonstrates that colonoscopy at ages 55 and 65 offers the best combination of reduction in colorectal cancer at the lowest cost. However, when compliance with screening recommendations is very high, costs are high, and the proportion of cancers arising from adenomas is low, the combination of FOS and FOBT is most cost effective. Malignant polyps look friable and irregular and feel hard. Sessile malignant polyps need to be treated by formal resection. Patients with pedunculated polyps with favorable histology (clear margin, well or moderately differentiated, no lymphovascular invasion) can be observed, and those whose polyps show unfavorable histology should have the polyp-bearing segment of colon resected along with its draining lymph nodes.

KEYWORDS: Colorectal cancer screening, colonoscopy, malignant polyp, histology

Objectives: Upon completion of this article, the reader should be familiar with colon cancer screening and management of the malignant polyp.

Citizens of western societies are particularly likely to develop colorectal cancer. Their diet and relatively sedentary lifestyle favor the accumulation of genetic changes in the colorectal epithelium that cause progressive neoplasia leading ultimately to adenocarcinoma.¹ This progressive neoplasia is usually asymptomatic and is not discovered until invasion has occurred. In 2005, the American Cancer Society predicts that ~145,290 people will be diagnosed with colorectal cancer in the United States and that ~56,290 people will die from it.² The average lifetime risk of colorectal cancer in the United States is 5.9%. Deaths from colorectal cancer are frustrating because they are largely

preventable. The change from normal mucosa to invasive neoplasm takes ~10 years, years in which the colon can be examined and the neoplasia found and removed before malignancy develops. Even if a cancer occurs, if it is found at an early stage the prognosis is good. Asymptomatic cancers are usually less advanced and more often curable than symptomatic ones.

The concept of investigating an asymptomatic organ to prevent the development of cancer or to diagnose early-stage disease is called "screening." Colorectal cancer is an ideal disease for the application of population-based screening as it is common, there is a lengthy premalignant stage, the premalignant adenomas

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are accessible and easily removable, and removal of adenomas or early cancers is likely to prevent death.³ Unfortunately, colorectal screening has found less acceptance among the public than screening for breast, prostate, and cervical cancer.⁴ Less than 30% of people older than 50 years have had a fecal occult blood test (FOBT) within the past 2 years, and only 20% have had a recent screening endoscopy.⁴ There are many possible reasons for this, including the distasteful nature of the large bowel as a topic of conversation, the embarrassment and discomfort associated with the screening tests, concern about coverage or reimbursement of the cost of the tests, and a degree of confusion about recommendations. A surge in public awareness of the problem of colorectal cancer⁵ has increased screening colonoscopy rates and has coincided with articles describing new screening technology and addressing the question of what test or combination of tests is most cost effective for colorectal cancer screening.⁶⁻¹⁰ The options have traditionally been FOBT, flexible sigmoidoscopy (FOS), and total colonic examination with either double-contrast barium enema (DCBE) or colonoscopy (CS). These options figure in the average risk screening recommendations published by several societies. Those recommended by the American Cancer Society are shown in Table 1.¹¹

Both FOBT and FOS have been shown in prospective studies to reduce death from colorectal cancer,¹²⁻¹⁵ and they have the advantages of being relatively inexpensive and noninvasive. However, both tests miss cancers and adenomas. Colonoscopy provides the most complete and accurate examination of the colon and rectum and allows concurrent treatment of adenomas, but it is expensive, has the highest complication rate, and has not been tested as a screening tool by a randomized trial. DCBE has the advantage of low cost but is considerably less accurate in diagnosing cancer or polyps than colonoscopy and has no therapeutic potential. The combination of fecal occult blood testing and sigmoidoscopy is more accurate in detecting significant colorectal neoplasia than either alone, without the expense or risk of total colonoscopy.¹⁵ However, the results are signifi-

cantly worse than could be achieved by colonoscopy alone. More recently publicized screening tests such as virtual colonoscopy and fecal DNA testing have yet to find wide acceptance because their accuracy is still poorly defined (virtual colonoscopy),^{6,7} because of their cost (fecal DNA testing),⁸ and because of the overriding advantage of colonoscopy: that abnormalities can be removed or biopsied at the same time.

RISK ASSESSMENT

The average lifetime risk for colorectal cancer in the United States is estimated as ~5.9%. Certain individuals have a higher risk, however, and these represent groups of people who should be a focus of screening efforts. The most important high-risk group is that with a positive family history of colorectal cancer. This group can be substratified into various levels of increased risk according to the strength of their family history. A recently described family history scoring system has been suggested for recognition and measurement of risk.¹⁶ Multiple first-degree relatives and colorectal cancer at a young (<50 years) age suggest dominant inheritance and even the possibility of hereditary nonpolyposis colorectal cancer.¹⁷

The second most important high-risk group comprises those with a personal history of colorectal neoplasia. These people have shown that their colorectal epithelium has accumulated enough mutations to produce at least one neoplasm, and the more advanced or more numerous the neoplasms, the higher the risk.¹⁸ Regular colonoscopy in this group is more properly termed surveillance.

The third most numerous high-risk group is at risk because of chronic colitis. This is classically ulcerative colitis but also includes Crohn's disease, even when the bowel has been diverted. Regular surveillance colonoscopy or proctoscopy with multiple biopsies to detect dysplasia is routine. Surveillance begins at ~7 or 8 years from onset of symptoms and continues at 2-year intervals until the disease has been present for 20 years, when yearly examinations are performed.¹⁹ There is little

Table 1 Recommendations of the American Cancer Society for the Screening of People at Average Risk for Colorectal Cancer¹¹

Test	Frequency (Starting at Age 50 years)	Comment
Fecal occult blood test (FOBT)	Yearly	If positive, colonoscopy
Flexible sigmoidoscopy	5 yearly	If a polyp is found, colonoscopy is recommended
FOBT and flexible sigmoidoscopy	Every year (FOBT) and 5 years	The combination is preferred over either test alone
Colonoscopy	Every 10 years	Assumes good bowel preparation and complete examination
Double-contrast barium enema (DCBE)	Every 5 years	If positive, colonoscopy The combination of flexible sigmoidoscopy and DCBE is better than either alone

Table 2 Results of Hemoccult Testing in Veterans Affairs Study

Colonoscopy Result	Hemoccult +ve	Hemoccult -ve
No polyp	84	1235
Non-neoplastic polyp	27	445
All neoplasia	128	966
Advanced neoplasia	73	231

+ve, positive; -ve, negative.
From Lieberman and Weiss.¹⁵ Reprinted with permission.

argument that regular colonoscopy is the best method of surveillance for all these high-risk groups. They are more likely than usual to produce an adenomatous polyp and so are more likely to need the biopsy and polypectomy options that colonoscopy offers. The question about which screening test is best relates exclusively to the very large number of people at average risk for colorectal cancer, who are unlikely to harbor an adenoma.

THE INDIVIDUAL TESTS

Fecal Occult Blood Test

There are three major, population-based, prospective, randomized trials of FOBT, each showing a reduction of mortality from colorectal cancer in the group having the test.^{12–14} The Minnesota study¹² was the only one to use rehydrated Hemoccult slides; it reported a 33% reduction in death from colorectal cancer for people having the test once a year and a 21% reduction if the test was done every 2 years. The Nottingham study¹³ and the Denmark study¹⁴ had reductions in mortality of 13%¹³ and 21%.¹⁴ Although FOBT may be effective at a population level, on an individual level its accuracy is low. Results of FOBT reported by Lieberman and Weiss¹⁵ are shown in Table 2. They show a positive predictive value (PPV) for advanced neoplasia of 31% and a negative predictive value (NPV) of 91%. For any neoplasia, the PPV is 54% and the NPV is 63%. Costs of the various screening options in 2001 were reported by Vijan et al.²⁰ and are summarized in Table 3. FOBT is a valuable screening tool because it is cheap and non-invasive. On a population level it is effective in saving

lives, although its accuracy in detecting advanced neoplasia is low.

Flexible Sigmoidoscopy

Selby et al.²¹ performed a case-control study showing that FOS is effective in reducing deaths from rectosigmoid cancers. However, much of the discussion of the value of FOS assumes that the examination reaches the splenic flexure and therefore examines half the colon.¹¹ This is an unrealistic assumption, and FOS screening has been decried as equivalent to performing screening mammography of one breast.^{22,23} Certainly, FOS is a compromise examination, historically based on the notion that most colorectal cancers are left sided and on the perception that the sigmoid colon is most difficult to examine with a barium enema. With the trend to more right-sided cancers and the increasing availability of endoscopic techniques to examine the entire colon, the relevance of FOS as a colorectal cancer screening tool is increasingly being challenged.

Combined Fecal Occult Blood Test and Flexible Sigmoidoscopy

Lieberman and Weiss¹⁵ in a Veterans Administration Hospital study enrolled 2885 subjects who both complied with Hemoccult testing and had colonoscopy, allowing a direct analysis of the accuracy of FOBT. The results of Hemoccult testing are shown in Table 2. The authors used the colonoscopy results to extrapolate data for inspection of the left colon and rectum alone and calculated the increase in sensitivity gained by adding FOS to FOBT. The sensitivity was significantly increased, although the combined screening approach still identified only 50.7% (76 of 150) of proximal advanced neoplasms.

Double-Contrast Barium Enema

The main problem with the use of DCBE as a screening tool is its lack of accuracy compared with colonoscopy, although this is most true for small polyps. However, the results of studies comparing colonoscopy with barium

Table 3 Costs of Screening Procedures and Treatment Of Colorectal Cancer

	Cost	With Biopsy/Polypectomy
FOBT	\$17 (5–30)	
FOS	\$225 (100–500)	\$240 (100–550)
FOS/FOBT	\$242 (105–530)	
Colonoscopy	\$550 (100–1000)	\$765 (200–1300)
Cancer treatment (Localized)	\$60,000 (40,000–80,000)	
Cancer treatment (regional)	\$82,800 (60,000–100,000)	

FOBT, fecal occult blood test; FOS, flexible sigmoidoscopy.
From Vijan et al.²⁰ Reprinted with permission.

enema depend on the perspective of the authors: radiologists tend to report data favoring radiology, and endoscopists produce data favoring endoscopy. Part of this is the unrealistic setting of trials performed carefully by experts in high-volume centers. Such data bear little relevance to routine service procedures performed in community hospitals. This dichotomy is also seen in reports of virtual colonoscopy. Bearing this in mind, a review of literature shows a wide range of sensitivities of DCBE in detecting colorectal polyps. For polyps less than 1 cm in diameter the sensitivity of DCBE ranges from 50% to 80%, whereas for polyps over 1 cm in diameter sensitivity can be as high as 90%.^{24,25} Other studies call in question the ability of DCBE to detect colorectal cancers with accuracy similar to that of colonoscopy. In a chart review study of 2193 consecutive patients with colorectal cancer in 20 central Indiana hospitals, Rex et al found that the sensitivities for detecting cancer were 95% for colonoscopy, 85.2% for DCBE, and 81.8% for single-contrast barium enema.²⁶ Using National Polyp Study data, Winawer et al reported miss rates for barium enema compared with colonoscopy of 65% for all polyps, 61% for all adenomas, and 52% for adenomas over 1 cm in size. Furthermore, there was a false-positive rate on barium enema of 18%.²⁷ Most recommendations for colorectal screening favor colonoscopy, although it is apparent that in the best of hands DCBE is almost as accurate for detecting large polyps or cancers.

Colonoscopy

Intuitively, colonoscopy seems to be the best choice for colorectal cancer screening. The colonic mucosa is examined under magnification and any abnormalities can be removed or biopsied. It is a direct examination, not radiological, and in 95% or more of cases the entire colon is examined. If colonoscopy is clearly the best way of screening for colorectal neoplasia, why is it not used as a routine? Detsky has suggested five reasons²⁸:

1. There is no large-scale, randomized study of colonoscopy screening.
2. Colonoscopy may be uncomfortable and unpleasant.
3. The risk of hemorrhage and perforation requiring surgery is ~0.1%.
4. Colonoscopy is too expensive.
5. There are not enough colonoscopists to satisfy the potential demand.

These concerns can be addressed as follows. First, large-scale, randomized studies to prove the efficacy of screening colonoscopy as a screening test are not needed. Surrogate data can be found in reports such as that by the National Polyp Study, which showed that when patients are kept adenoma-free, the incidence of colorectal cancer

falls considerably,³ and in reports by the large-scale Hemoccult studies, which showed that when cancers were found at an early stage, survival was improved.¹²⁻¹⁴ The same effects can be expected when colonoscopy is the primary screening technique. Second, the pain associated with colonoscopy may be overstated. We have found it to be severe in only 9% of cases.²⁹ Sedation is usually given, and the test need be endured only once every 8 to 10 years. Many patients complain of more pain during FOS than colonoscopy. Furthermore, radiologic studies such as barium enema and virtual colonoscopy can also be painful, and no sedation is given for these tests. Third, the risk of complications during diagnostic colonoscopy is tiny.³⁰ The often-quoted high rates of hemorrhage (0.04%) and perforation (0.08%)³¹ date from times when colonoscopes were larger, more rigid, and more difficult to use than the soft, narrow, supple scopes we use today.

The fourth point raised by Detsky is the most telling. In a survey of charges for medical procedures in the United States and Canada, the range of colonoscopy charges was \$198.51 to \$3554.³² The median charge in the United States was \$1736 and in Canada was \$606. For colonoscopy to be cost efficient as a screening test, Frazier et al concluded that it should cost \$780.³³ The level of reimbursement paid by Medicare for colonoscopy is about \$600, including both technical and professional charges. Charging for screening colonoscopy at a discounted price may be necessary for it to be more widely accepted as a routine screening test by private insurers and patients. Finally, the availability of colonoscopists is also likely to be a limiting factor in the adoption of widespread colonoscopy screening. Seeff et al surveyed ~1800 practices from a list of 8207 known to have purchased or leased endoscopic equipment and calculated that in 2002, ~2.8 million flexible sigmoidoscopies and 14.2 million colonoscopies were performed in the United States. Practices felt they could increase these numbers to 9.5 million sigmoidoscopies and 22.4 million colonoscopies.³⁴ When this potential increase in capacity is viewed in light of the 41.8 million Americans older than 50 years who have not yet been screened for colorectal cancer,³⁵ the challenge of keeping up with recommendations is obvious. The stress that these extra examinations would place on the system has implications for quality control. Colonoscopy is a demanding procedure, difficult to learn and difficult to do well. Expertise is an amalgam of talent, training, and experience and needs to be measured by factors other than the traditional completion rate. Patients' comfort, morbidity and mortality, and accuracy of diagnosis are all dependent on the expertise of the colonoscopists but are hard to measure and are rarely reported. There is a real danger that wholesale adoption of colonoscopy as the preferred screening technique for colorectal cancer will result in many inaccurate, painful, and dangerous examinations.

It is up to the societies that train, monitor, and credential colonoscopists to guard against such a development.

Virtual Colonoscopy

Over the past 10 years, virtual colonoscopy has been increasingly and aggressively promoted as an alternative to conventional colonoscopy for colorectal cancer screening. Its advantages are similar to those of DCBE, including a noninvasive technique with no need for sedation. Its potential exceeds that of DCBE as advances in technology and software may allow more standardized reading of the scans, easier detection of adenomas, and complete avoidance of laxative bowel preparation. Studies comparing virtual and conventional colonoscopy show conflicting results. Pickhardt et al found the two tests to be equivalent, or slightly in favor of virtual colonoscopy, in terms of sensitivity for tumors 1 cm in diameter or larger,⁶ whereas the comparison reported by Cotton et al favored conventional colonoscopy.⁷ It is agreed that at present virtual colonoscopy is relatively insensitive for small and diminutive polyps, but the reaction of some radiologists has been to downplay their clinical significance.³⁶ However, a study of small and diminutive adenomas has shown a 4.5% incidence of advanced adenomas (> 25% villous architecture or severe dysplasia).³⁷ This means that small or diminutive adenomas cannot just be ignored. There is a role for virtual colonoscopy in colorectal cancer screening, especially if the accuracy becomes more uniform across centers, if it can be done without bowel preparation, and if it is restricted to patients at low risk for having polyps.

Fecal DNA

In 2004 an article appeared reporting the results of the first large population-based study of colorectal cancer screening using a panel of genetic markers to identify mutations in fecal DNA.⁸ Fecal DNA analysis had a sensitivity of 51.6% for cancer (compared with 12.9% for FOBT) and 18.2% for advanced adenomas (compared with 10.8% for FOBT).⁸ Although the test is commercially available, its relatively low sensitivity and relatively high cost will prevent it from becoming the first-line colorectal cancer screening tool at a population level. More than any other test, however, it is capable of improving sensitivity and decreasing cost as advances in genetic knowledge and technology can be brought to bear.

Summary

In determining the best tests or combination of tests for colorectal cancer screening, the important factors to consider are the percentage of cancers arising from polyps (and therefore preventable by polypectomy), the

likely compliance with the proposed test, the cost of the test, and the benefit in lives saved or cancers prevented. It is likely that over 80% of cancers arise in preexisting adenomas, a contention supported by data from the National Polyp Study showing a dramatic drop in the incidence of colon cancer in patients kept adenoma free for 7 years.³ Compliance with colorectal cancer screening outside randomized studies has been found to be as low as 48.4% for FOBT, 62.2% for digital rectal examination, and 33.1% for proctoscopy.³⁸ The estimated costs of common screening examinations and of treatment of colorectal cancer are given in Table 3 and the sensitivity of the tests in Table 4.²⁰

The result of integrating all these factors in terms of lives saved and the cost per life saved was reported by Vijan et al.²⁰ They showed that colonoscopy at ages 55 and 65 offers the best combination of reduction in colorectal cancer at the lowest cost. When compliance with recommendations is very high, costs are high, and the proportion of cancers arising from adenomas is low, the combination of FOS and FOBT is most cost effective. However, when compliance is low, if cancers usually arise from polyps, and when costs are held to a reasonable level, colonoscopy is the most cost-effective screening technique.²⁰ These calculations do not include virtual colonoscopy or fecal DNA testing, but these will factor into compliance and cost considerations. At present, the best we can do for our patients is to present them with the need for colorectal cancer screening, the rationale behind it, a personal risk assessment, and personalized recommendations for screening based on risk. For patients at average risk the screening options need to be defined, along with their advantages, disadvantages, and the likelihood of false-positive and false-negative results. The patients may then choose, according to their financial circumstances and their personal preference. The first priority is to get all Americans to consider colorectal cancer screening. The second priority is to recommend the most cost-effective choice. This may include accepting realistic reimbursement for colonoscopy while at the same time persuading third-party payers to cover the test.

Table 4 Summary of Sensitivity of Screening Tests for Colorectal Cancer or Polyps

	Sensitivity for Polyps	Sensitivity for Cancer	For "Advanced Neoplasia"
FOBT	5% (2–10)	30% (20–40) 50% (40–60)	10%–24%
FOS			70%
FOS/FOBT			76%
Colonoscopy	85% (80–95)	95% (90–100)	
Fecal DNA ⁸	55%–93% ^{6,7}	52%	18%

FOBT, fecal occult blood test; FOS, flexible sigmoidoscopy.
Modified from Vijan et al.²⁰

The future holds promise for revolutions in colorectal cancer screening. In addition to improvements in fecal DNA testing, testing blood for cancer-predisposing genetic polymorphisms may be an effective way of determining individual risk.³⁹ The more we can perform accurate risk assessment, the more focused colonoscopy can be and the more available and cost effective it will be. FOBT and FOS are too inaccurate. Because of the extra diagnostic and therapeutic options it offers, colonoscopy is the ultimate screening tool, as long as we can schedule it and pay for it.

THE MALIGNANT POLYP

A colorectal adenoma is a benign neoplasm developing in the colorectal mucosa as a result of genetically mediated loss of control of cell growth, differentiation, and death. It is a precursor to invasive neoplasia or malignancy. Sometimes an adenoma is removed endoscopically after malignant transformation has occurred. Typically, the polyp looks benign or is benign appearing enough to encourage the colonoscopist to continue with plans to remove it. The real nature of the lesion is revealed only by histology, and the clinician is then faced with advising a patient who has had a malignant polyp removed some days previously. There are two possible courses of action: to make sure the polyp is completely removed but then to follow the patient endoscopically or to recommend formal resection of the bowel that had harbored the polyp. Observation is associated with low morbidity and mortality, avoids pain and time off work, but runs the risk of allowing residual cancer to grow and possibly to metastasize. Surgery excludes the risk of spreading cancer but carries the risk of postoperative complications and the certainty of some pain and some convalescence. There are criteria that predict which patients are at risk of having residual cancer and which are not. This section discusses these criteria.

Definition

The definition of a malignant polyp is theoretically straightforward but in practice can become confused. An adenoma contains dysplastic cells, whose appearance suggests loss of cellular growth and reproduction control. Mildly dysplastic cells show mild changes such as nuclear darkening and palisading. Severely dysplastic cells show even darker but irregular nuclei. These cells are similar to cells seen in a cancer, but until they penetrate the muscularis mucosae to enter the submucosa, the polyp is benign; the dysplastic cells cannot spread.¹ An adenoma with severe dysplasia where the dysplastic cells are confined by the basement membrane of the glands is the same as an adenoma with "carcinoma in situ"; the terms are synonymous and polypectomy is curative.¹ Another term, intramucosal adenocarcinoma, refers to

an adenoma where the severely dysplastic cells enter the lamina propria (the supporting tissue of the mucosa between the glands) but are confined to the mucosa by the muscularis mucosae. This is also a benign polyp, curable by polypectomy.¹

Unfortunately, pathologists differ in their ability to interpret adenoma histology, as shown by Komuta et al.⁴⁰ Three pathologists performed a blinded review of histology from 76 malignant adenomas and 12 adenomas with carcinoma in situ. Although the three reviewers agreed substantially in defining stage, status of the resection margin, and depth of invasion, there was only moderate agreement with the original pathology report. Furthermore, even the experts failed to agree when reporting differentiation and angiolymphatic invasion. Others have reported similar findings. Rex et al randomly selected 20 general pathologists in community practice and asked them to review the slides of 20 colorectal polyps. Only 55% of reports commented on the differentiation of malignant polyps, and the status of the margin was described in only 50%.⁴¹ High-grade dysplasia was reported correctly in 47%, was called invasive cancer in 22%, and was missed in 31% of reports.⁴¹

Therefore, the first step in the management of a malignant polyp is to confirm the histology, either by looking at the slides personally or by having them checked by another experienced pathologist. Otherwise, it is possible that a major bowel resection may be performed unnecessarily.

Recognizing a Malignant Polyp Endoscopically

It is helpful if a colonoscopist can develop the ability to distinguish malignant polyps from benign ones. This would help to prevent the difficult scenario of a surgeon being referred a patient who had a high-risk malignant polyp somewhere in the colon, but the precise location is not known, the polypectomy site has healed, and the extent of the proposed resection has to be enlarged to make sure that the right segment of bowel is included. A colonoscopist who knows that a particular polyp has a high chance of being malignant can pay close attention to defining the site as precisely as possible, possibly tattooing the area, and making sure that the pathology report and the surgical consultation are not delayed.

Although some malignant polyps look benign, typical signs that there is some invasion include hardness, loss of mobility of the polyp over the underlying bowel wall, and irregularity and friability of the epithelium.⁴² Sessile polyps suspicious for cancer should not be snared as the risk of perforation is enhanced by the penetration of the malignancy into the bowel wall.

Table 5 Recent Studies Reporting Outcome of Treatment of Malignant Colorectal Adenomas According to Prognostic Factors

Author	Year	Unfavorable Histology	Favorable Polyps with Adverse Outcome	Unfavorable Polyps with Adverse Outcome
Cooper ⁴⁶	1995	Tumor at or near margin +/- Gd III histology +/- lymphatic/venous invasion	0/46	14/71 (19.7%)
Volk ⁴⁴	1995	Margin not assessable or < 2 mm +/- Gd III histology	0/16	10/30 (33%)
Hackelsberger ⁴⁷	1995	Incomplete excision Gd III histology	0/42	7/34 (21%)
Netzer ⁴⁵	1998	Incomplete polypectomy, Margin not clearly cancer free Gd III histology Lymphatic or venous invasion	0/32	16/38 (42%)
Seitz ⁴⁸	2004	Involved margin Gd III histology Vascular invasion	0/54	14/52 (27%)
Total			0/190	61/225 (27%)

Gd, grade.

Prognostic Factors

When the presence of invasion of the muscularis mucosae by malignant cells is confirmed, the decision to resect or observe is based on two considerations; the chances of residual cancer in the bowel wall and the chances of nodal metastases. It is possible to evaluate the chances of residual cancer only in a pedunculated polyp. Malignant sessile polyps always need formal resection, as it is impossible to orient the specimen to evaluate margins and there is no separation between polyp and bowel wall. Using the levels of invasion described by Haggitt et al,⁴³ every malignant sessile polyp is level 4. A stalk provides a degree of separation of polyp from bowel wall and allows easy orientation of the specimen so that the margin can be examined. Patients with malignant pedunculated polyps with a suitable margin between cancer and the cut end of the stalk can therefore be observed with confidence that no mucosal cancer remains. Volk et al determined the suitable margin to be 2 mm,⁴⁴ although there is some debate about this.

The best indicator of the possibility of nodal metastases is the differentiation of the malignant cells. Poorly differentiated cancers (grade III) have a much higher chance of nodal spread and should all be resected formally. Moderately or well-differentiated cancers have a significantly lower chance of nodal metastases and can be observed.

Other histologic criteria such as the presence of venous or lymphatic invasion offer little extra predictive ability over differentiation, although they have been used to define malignant polyp histology as favorable or unfavorable. When angiolymphatic invasion is present, other adverse factors are almost always present as well.^{45,46}

Although there are many studies examining the outcome of endoscopic resection of a malignant polyp, criteria for defining favorable and unfavorable histology have only relatively recently become uniform. Some

studies are summarized in Table 5.^{47,48} This table shows that the status of the margin and the grade of histology are standard; the presence of lymphatic or venous invasion is commonly used but not universal.

The use of a 2-mm margin in defining favorable histology is controversial. Netzer et al⁴⁵ reported that 28% of their patients with a clear margin had cancer within 2 mm of the cut end of the stalk, and all had a favorable outcome. The difference between 1 mm and 2 mm in a polyp with well or moderately differentiated cancer seems unlikely to be clinically important as long as the margin is clean and the histologic clearance is clear. Whatever definition is used, the gastroenterologist and surgeon evaluating a patient with a malignant polyp must be assured that the margin of resection is clear of cancer before a decision against surgery can be taken. Table 5 shows that when the margin of resection is clear and the differentiation of the tumor is mild or moderate, an adverse outcome from endoscopic resection and observation is extremely unlikely.

Surgical Morbidity

The other factor influencing the decision to resect or to observe is the likely morbidity and mortality of surgery. This is determined by patient-related factors and by the skill and experience of the surgeon. Patient-related factors such as age and comorbidities may make surgical resection prohibitive. The 30-day mortality from a resection for colorectal cancer can be anticipated to range from less than 1%⁴⁹ to over 15%,⁵⁰ depending on factors such as the patient's age and comorbidity and the nature of the surgery (emergency versus elective). Overall post-operative complications rates of 20% are standard,⁴⁹ and serious complications such as anastomotic leak can occur in 3% to 5% of cases.⁵¹ Table 5 shows that the chance of residual tumor after excision of an unfavorable malignant adenoma is 27%, making surgical resection preferable in

all but the highest risk patients. The popularization of laparoscopic techniques has minimized the pain and disability associated with surgery,⁴⁹ tilting the balance further in favor of resecting the colon when there is an unfavorable adenoma. However, laparoscopy also provides the opportunity for error such as removal of the wrong section of bowel.

Summary

A malignant polyp usually looks more friable and more irregular and feels harder than its benign precursors. Such polyps need to be accurately localized during colonoscopy. When malignant polyps are reported, a review of the histology is worthwhile. Sessile malignant polyps need to be treated by formal resection. Pedunculated polyps are categorized as having favorable histology (clear margin, well or moderately differentiated, no lymphovascular invasion) or unfavorable histology. Patients with favorable polyps can be observed; those with unfavorable polyps should have the polyp-bearing segment of colon resected along with its draining lymph nodes.

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